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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/627,600	07/28/2000	Samuel R. Denmeade	57109 (71699)	3631

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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/627,600	DENMEADE ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003 and 12 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 57-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-56* is/are rejected.

7)☒ Claim(s) *23 and 30-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-62 are pending.

Applicants' amendment filed 2 June 2003, which amends claims 8, 28 and 29 has been entered.

Election/restriction

Applicants' election (filed 12 August 2004) of Group IV, claims 17-56 is acknowledged. Because applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-16 and 57-62 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions. Therefore, the pending claims 17-56 are under examination to the extent that they are drawn to the elected invention.

IDS

The references listed in IDS filed 20 February 2001, IDS filed 15 January 2002, and IDS filed 11 June 2003 have been considered by Examiner.

Specification/Claim/ Objections

The disclosure is objected to because of the following informalities:

(1) Claim 23 is object to because "SERCA" should be spelled out for the first time recitation in the claims.

Claims 30-31 are object to because the claim recitation "IC_{50}" is inconsistent with the specification where sets forth "LC_{50}" instead.

(2) In page 2, the last line, "Fig. 1" should be changed to "(see Figure 1)".

(3) In the first page, before the specification, the application should indicates that this application claims benefit of provisional application 60/146316 filed 29 July 19999.

(4) In page 13, line 10, the phrase "C-2 or C-8 carbon" should be clarified; and line 16, "LC50" should be changed to "LC_{50}".

(5) In page 17, line 27, "BSA" should be spelled out in full for the first instance of use.

(6) In page 21, line 7, the sequence "Ala-Arg-Arg-AMC" lacks sequence identifier following it.

(7) In page 21, line 18, the phrase "The Dixon plot 1/v" should be clarified. Note that the Dixon plot is a way of calculating the K_i of an inhibitor wherein a graph of the reciprocal of velocity against inhibitor concentration is plotted.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, the second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 17-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite for depending from claim 1 which is non-elected. See also claims 37 and 48. The dependent claims are also rejected.

Claim 24 is indefinite because the claim contains an open ended Markush group (see "or thapsigargin derivatives"). Markush language requires close language.

Claim 29 recites the limitation "the peptide linker". There is insufficient antecedent basis for this limitation in claim 17 from which claim 29 depends. Claim 29 is indefinite because the claim contains an open ended Markush group. See "... amido- or amino-substituted ..."; wherein "or" renders the recited Markush group open. Markush language requires close language. Also, "and" before "CO-$(CH_2)_{n3}$-NH-CO-CH(R_4)-NH_2" renders the claim 29 indefinite because there should be only one amino-substituent recited.

Claim 40 is unclear in "the linker comprises Leu" because claim 39 from which claim 40 depends does not expressly set forth that the linker is a peptide, i.e., said linker refers broadly to an organic moiety (not necessarily being a peptide moiety). Thus, claim 40 must make it clear that (i) whether or not "Leu" refers to leucine, and (ii) how the linker comprises leucine amino acid.

Claim 41 recites the limitation "the group". There appears to be insufficient antecedent basis for this limitation in the claim. Suggest "the capping group".

Claim 43 recites "a hK2-producing cell proliferative disorder" appears to be awkward and unclear; does it refer to that said proliferative disorder is caused (produced) by hK-2 cell? The dependent claims are also rejected.

Claim 48 recites the limitation "the detectable label". There appears to be insufficient antecedent basis for this limitation in the claim. Does said detectable label is the detectably labeled peptide recited in claim 48? The dependent claims are also rejected.

Conclusion

No claims are allowed.

Prior Art

The prior art made of record and not currently relied upon in any rejections is considered pertinent to Applicants' disclosure. Yet, it is of note that the following patent claiming a benefit to Application No. 09/588822 (now US Patent No. 6504014) does not disclose a composition comprising a prodrug comprising a drag linkage to a peptide which is specifically cleaved by *human kallikrein 2* (hk2) enzyme); and thus, priority date of 6504014 is considered not beyond its filing date 28 July 2000.

Isaacs et al. (US Pat. No. 6545131) teach a composition comprising a prodrug that comprises a therapeutic drug and a peptide; wherein said peptide is linked to said drug and release of said drug from the peptide is accomplished by a selectively proteolytic cleavage of the peptide by human kallikrein 2 (hK2) enzyme (see column 10, line 67 to column 11, line 5).

In column 11, lines 54-57, Isaacs et al. teach that the peptide is linked to a primary amine group of the drug molecule.

In column 25, lines 10-28, Isaacs et al. teach a peptide linker comprising leucine for linkage between the peptide and the drug molecule.

In column 8, lines 21-47, Isaacs et al. teach that the therapeutic drug delivered to the target tissue inhibits endoplasmic reticulum calcium-ATPase (SERCA) pump.

Isaacs et al. teach that the therapeutic drug is thapsigargin (see column 8, lines 37-47).

In column 8, lines 21-37, Isaacs et al. teach that the therapeutic drug is an anthracycline antibiotic, e.g., idarubicin (4-demethoxydaunomycin), which is capable of intercalating into polynucleotides.

In Example 16, Isaacs et al. teach an ability of thapsigargin of inhibiting endoplasmic reticulum Calcium-ATPase (i.e., SERCA); and, in column 13, paragraphs 5-6, Isaacs et al. teach that the drug has the IC_{50} value toward endoplasmic reticulum calcium-ATPase of at most 500nM or 50nM, as applied to the instant claims 30 and 31, respectively; or at most 20 μM, as applied to the instant claim 32; or at most 5 μM which value is less than 2.0 μM.

In column 6, lines 53-54, Isaacs et al. teach that the therapeutic drug is water soluble.

In column 15, lines 29-34, Isaacs et al. teach that the composition additionally comprises polysaccharide, e.g., cyclodextrin.

Additionally, in columns 14-15, Isaac et al. teach a method of producing a prodrug comprising linking a therapeutic drug and a peptide wherein activity of the linked drug is inhibited.

Isaacs et al. teach that the peptide is linked to a primary amine group of the drug molecule (see column 15, lines 5-9), and that a peptide linker comprising leucine for linkage between the peptide and the drug molecule (see column 15, lines 21-27).

Isaacs et al. teach that the composition contains conventional capping groups, e.g., glutaryl substituent, connected to the amino terminus of the peptide to prevent endopeptidase activity from degrading said peptide (see column 6, lines 56-61).

In "Summary of the invention" section (column 2), Isaacs et al. teach a method of treating *cell proliferative disorders* comprising administering to the subject a therapeutically effective amount of the composition sated above.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel Wei Liu, Ph.D.
Art Unit 1653, Examiner
September 17, 2004

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER